VACCINE UPDATE

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WRHA
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PLAN

1. Pneumococcal Vaccines: recent changes
2. Hot Topics in Vaccines:
   • adjuvants
   • rotavirus vaccine
   • antipyretics and vaccines

Pneumococcal Vaccines: Significant Changes are Afoot
Pneumococcal Disease

- *S. pneumoniae* first isolated by Pasteur in 1881
- Confused with other causes of pneumonia until discovery of Gram stain in 1884
- Polysaccharide capsule important virulence factor
- Type-specific antibody is protective

PNEUMOCOCCAL INFECTION

Non-invasive disease
- Sinusitis (sinuses)
- Otitis media (middle ear)
- Pneumonia (lungs)

Invasive disease
- Bacteremia (blood)
- Meningitis (CNS)
- Endocarditis (heart)
- Peritonitis (body cavity)
- Septic arthritis (bones and joints)
- Others (appendicitis, salpingitis, soft-tissue infections)
Nasopharyngeal carriage may occur in up to 80% of healthy pre-school children and up to 30% of healthy older children and adults.

Nasopharynx: site of colonisation

Inhalation

Patient with pneumococcal disease

Asymptomatic carrier

Nasal cavity

Trachea

Dissemination

Nasopharyngeal carriage of Pneumococcus

Burden of Pneumococcal Disease in Children*

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteremia</td>
<td>13,000</td>
</tr>
<tr>
<td>Meningitis</td>
<td>700</td>
</tr>
<tr>
<td>Death</td>
<td>200</td>
</tr>
<tr>
<td>Otitis media</td>
<td>5,000,000</td>
</tr>
</tbody>
</table>

*Prior to routine use of pneumococcal conjugate vaccine
Conditions That Increase Risk for Invasive Pneumococcal Disease

- Decreased immune function
- Asplenia (functional or anatomic)
- Chronic heart, pulmonary, liver or renal disease
- Cigarette smoking
- Cerebrospinal fluid (CSF) leak

Children at Increased Risk of Invasive Pneumococcal Disease

- Functional or anatomic asplenia, especially sickle cell disease
- HIV infection
- Recipient of cochlear implant
- Out-of-home group child care
- African American children
- Alaska Native and American Indian children who live in Alaska, Arizona, or New Mexico
- Navajo children who live in Colorado and Utah
PNEUMOCOCCAL DISEASE

- Invasive pneumococcal disease is serious and has a high risk of mortality
- Risk factors include old age, chronic illness, asplenia and immunodeficiency
- Mortality remains high despite appropriate antibiotic therapy
- *S. pneumoniae* resistance to antimicrobials is increasing
  (with concomitant increasing cost of management)

Prevention of pneumococcal disease among high-risk groups is a priority

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Invasive Pneumococcal Disease
Incidence by Age Group, 1998 and 2002

<table>
<thead>
<tr>
<th>Age Group (Yrs)</th>
<th>1998</th>
<th>2002</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td></td>
<td>50</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td>100</td>
</tr>
<tr>
<td>1-4</td>
<td>25</td>
<td>150</td>
</tr>
<tr>
<td>5-17</td>
<td>15</td>
<td>200</td>
</tr>
<tr>
<td>18-34</td>
<td>10</td>
<td>250</td>
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<tr>
<td>35-49</td>
<td>5</td>
<td>150</td>
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<tr>
<td>50-64</td>
<td>2</td>
<td>100</td>
</tr>
<tr>
<td>65+</td>
<td>1</td>
<td>5</td>
</tr>
</tbody>
</table>

* Rate * Rate per 100,000 population
Source: Active Bacterial Core Surveillance/EIP Network

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CCDR 2006; 32(14)
IPD in BC in < 3 y/o (2002 – 2006)

IPD in Calgary Infants 0 – 23 mo. (1998 – 2007)

IPD Calgary ≥ 65 y/o (1998 – 2007)

Herd immunity (or community immunity)

- describes a type of immunity that occurs when the vaccination of a portion of the population (or herd) provides protection to unvaccinated individuals. (John TJ, Samuel R, 2000)
- This is accomplished because, by having a large percentage of the population vaccinated, it reduces the spread of the pathogen within the community.
- Unvaccinated individuals can be individuals in older age groups like in the pneumococcal example.
- It can also be in groups that can’t be vaccinated, ex. newborns or those with chronic illnesses or individuals allergic to vaccines

Pneumococcal Conjugate Vaccines

- Current pneumococcal vaccines
  - conjugate with diphtheria CRM197 protein: Prevnar®, 7 valent (provides coverage against 7 strains of pneumococcal)
  - 23 valent polysaccharide vaccine: Pneumovax® 23, Pneumo 23®

Proportion of pediatric pneumococcal disease prevented by vaccination
**Recommendation for Polysaccharide Pneumococcal Vaccine**

- Healthy elderly people (> 65 years of age), particularly those living in institutions
- Patients with chronic cardiopulmonary disease, DM, alcoholism, chronic liver disease, CSF leak
- Particular immunodeficiencies
- Children with high risk- sickle cell anaemia or splenectomized

**Problems with polysaccharide vaccine in children**

- Not effective in children less than 2 years
- No effect on nasal carriage
- No herd effect
- Absence of immunologic memory
- Antibody level to several serotypes decline to pre-vaccination values within 3-7 years corresponding to a decline of clinical protection

**Pneumococcal Conjugate Vaccines (2)**

- New to market (May 2009):
  - Synflorix™
    - 10 valent conjugate vaccine
    - Novel carrier (H. influenza protein D)
Purpose of Protein D Carrier?

1. minimize potential for carrier-mediated immune interference
2. protect against major acute otitis media pathogens – pneumococcus and non-typeable *H. Influenzae*
Proportion of pediatric pneumococcal disease prevented by vaccination

**10-valent**

Assumes cross protection within serogroup 6

<table>
<thead>
<tr>
<th>Region</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Region A</td>
<td>88%</td>
</tr>
<tr>
<td>Region B</td>
<td>84%</td>
</tr>
<tr>
<td>Region C</td>
<td>66%</td>
</tr>
<tr>
<td>Region D</td>
<td>81%</td>
</tr>
<tr>
<td>Region E</td>
<td>81%</td>
</tr>
<tr>
<td>Region F</td>
<td>81%</td>
</tr>
</tbody>
</table>

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**PCV-10 (Syndflorix)**

- 10 valent conjugate vaccine
- Novel carrier (H. influenza protein D)
  - May protect against non-typeable Hi disease
- Efficacy proven against acute otitis media
- **Impact:** minimal advantages except in certain jurisdictions (e.g. Nunavut, Northern Alberta) infants with repeated otitis media?

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**Pneumococcal Conjugate Vaccines (3)**

- **PCV13: Prevnar® 13**
  - 13 valent conjugate vaccine with diphtheria CRM197 protein
  - licensed in Canada December 2009
  - proposed indications – prevention of:
    - invasive pneumococcal disease
    - pneumonia
    - otitis media
  - **Impact:** replaces Prevnar® 7 broader coverage with more relevant serotypes
- **FPT governments to determine product**
Serotype Composition

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>4</th>
<th>6B</th>
<th>9V</th>
<th>14</th>
<th>18C</th>
<th>19F</th>
<th>23F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevnar®</td>
<td>4</td>
<td>6B</td>
<td>9V</td>
<td>14</td>
<td>18C</td>
<td>19F</td>
<td>23F</td>
</tr>
<tr>
<td>Synflorix™</td>
<td>4</td>
<td>6B</td>
<td>9V</td>
<td>14</td>
<td>18C</td>
<td>19F</td>
<td>23F</td>
</tr>
<tr>
<td>Prevnar® 13</td>
<td>4</td>
<td>6B</td>
<td>9V</td>
<td>14</td>
<td>18C</td>
<td>19F</td>
<td>23F</td>
</tr>
</tbody>
</table>

Proportion of pediatric pneumococcal disease prevented by vaccination

- **13-valent**
  - Proportion: 92%, 89%, 87%, 87%, 86%

Changing Epidemiology

- Pediatric PCV7 programs in Canada produced a > 80% decline in pediatric IPD
- Herd immunity benefits in adults
- Incidence of non-vaccine serotypes has increased (so lesser reduction in overall incidence of IPD)
- 2004-2009: widespread community-based outbreak of serotype 5 in adults in western Canada
- Increasing incidence of disease due to serotype 19A, including multidrug resistant 19A
(A) Pneumococcal mastoiditis cases caused by serotype 19A among children at Texas Children's Hospital between 1995 and June 2007.
(B) Pneumococcal isolates and the proportion that were serotype 19A recovered from middle ear fluid cultures obtained from children at Texas Children's Hospital between 1995 and June 2007.

![Graph showing the percentage of isolates with serotypes included in the vaccine surveillance system](image)

![Graph showing the percentage of isolates causing IPD in children aged 6 months to 5 years of age during 2007 and 2008 with serotypes included in different conjugate vaccines](image)

Percentage of isolates causing IPD in children aged 6 months to 5 years of age during 2007 and 2008 with serotypes included in different conjugate vaccines

![Bar chart showing the percentage of isolates with serotypes included in different surveillance systems](image)
Summary

- 2 new conjugate vaccines against *Streptococcal pneumoniae* disease
- significant differences in carrier protein with additional benefits
  - e.g. acute otitis media
- changing epidemiology of IPD may drive choice of product
- degree of cross-protection from PCV7 and PCV10?

Hot Topics in Vaccines

Take Home Message?